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<p>The purpose of the present study was to examine electrophysiologically the effect of laser induced retinal lesions on the visual cortex of mammalian animal model. The effect of threshold energy levels of laser radiation was studied acutely and chronically in cats using the visual evoked response (VER). In addition, electroretinographic (ERG) studies have been added to the program to obtain direct physiological evidence on the condition of the retinal area affected by the laser radiation. This study was coordinated with LAIR personnel (The P.I. visited two times in LAIR), especially with regard to the type of laser technology to be used and its availability in the Goldschleger Eye Institute. A Neodymium YAG laser device (Nd:YAG) was used; energy levels applied were 0.1-1.0 millijoules (mJ) and 1-100 pulses were given to the various cats. The results showed that the ERG is affected; the lased eye was less excitable than the normal eye in most of the cats studied, whatever laser energy has been applied. The findings of the visual evoked response (VER) showed that in most cats the lased eye was inferior to the normal eye. An effect was found even in cases where energy level was as small</p>					
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as 0.1 mJ and whether the animals were exposed to the laser radiation 1 day or 6 weeks prior to the recording session. In conclusion, in view of the morphological and histological findings observed in our lased cats, the energy levels applied have an effect on information processing in the visual system. It can be concluded from the intensity of the responses, however, that although the ERG and VER indicate a retinal damage, they can not be used as diagnostic tools in determining laser induced damage, despite the fact that this damage has an effect on vision in the central region of the visual field. However, the ERG and VER can be used for the determination of low level laser power effects only if supported by data from other paradigms which may give evidence on the efficiency of pattern vision via the lased eye.

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Laser Retinal Effects: Electrophysiological Determination in Visual
Cortical Cells of Monkeys and Cats

Final Report

Prof. Uri Yinon

June 25, 1989

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Summary

The purpose of the present study was to examine electrophysiologically, during a one-year period, the effect of laser induced retinal lesions on the visual cortex of a mammalian animal model. More specifically, the effect of threshold and subthreshold levels of laser radiation on animals was studied both acutely and chronically. The effect of low level laser induced retinal lesions on retinal receptive fields of single cortical cells in cats and monkeys as well as the effect of these lesions on the visual evoked response (VER) were the subject of the original proposal. However, due to technical limits on the ability to incorporate a laser system into our stimulating optical system for on-line studies of the cellular response, off-line studies of the cortical evoked response were performed. We have thus studied the effects on visual evoked potential changes with regard to both threshold responsiveness of the primary visual cortex (area 17), and to the understanding of the visual processes altered by laser radiation.

In addition, electroretinographic studies were added to the program for two main reasons: 1) To obtain direct physiological evidence regarding the condition of the retinal area affected by the laser radiation; it was expected that in cases of extensive retinal damage, this would be indicated by the retinal response; 2) Since the ERG is currently used as an electrodiagnostic tool, it was also presently decided to study whether changes take place specifically in its main components as a result of the retinal induced lesions.

This study was coordinated with LAIR personnel (the PI has visited two times in LAIR and met several more times with LAIR personnel in the States and in Israel), especially with regard to the current limitation in the laser facilities of the Goldschleger Eye Institute.

A Neodymium YAG laser device (Nd:YAG) in the possession of the Ophthalmology Department of the Goldschleger Eye Institute was used, under special permission and constant supervision of an ophthalmologist. Energy levels were in the range of 0.1-1.0 millijoules (mJ) per pulse and 1-100 pulses were applied in the various groups of cats.

The results show that the retinal response (ERG) is affected; the lased eye was less efficient than the normal eye in most of the cats studied. This finding is applicable to the affected eyes, whatever laser energy was applied, indicating that even the lowest doses applied exceeded the threshold for physiological effects. It can be concluded from the intensity of the ERG response, that retinal damage has occurred, however, it can not be used as diagnostic tool in determining the extent of laser induced damage, or even for determining whether vision in the central visual field has been affected.

The findings of the visual evoked responses (VER) showed that in most cats the lased eye was inferior to the normal eye with regard to the cortical response. An effect was found even in cases where the energy level was as small as 0.1 mJ. An effect was found whether the animal was exposed to the laser radiation 1 day or 6 weeks prior to the recording session. However, the differences obtained between the lased and the normal eye do not seem to suggest that the flash evoked response can be used as a sole diagnostic test to determine the extent of laser retinal induced damage.

In conclusion, in view of the morphological and histological findings observed in the lased cats, the energy levels applied have an effect on information processing in the visual system. However, the visual evoked response can be used for the determination of low level laser power effects only if supported by data from other paradigms which may give direct evidence on the efficiency of vision via the lased eye.

Foreword

In conducting the research described in this report, the investigator adhered to the "Guide for the Care and Use of Laboratory Animals", prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, Commission of Life Sciences, National Research Council (NIH Publication No. 86-23, Revised 1985).

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Introduction

The extent of exposure to laser radiation has undoubtedly increased in the recent years with the appearance of more laser associated weapons in the battle field. Under these conditions, over exposure of the eyes to laser radiation causes damage to the retina and, if foveal, may result in a severe loss of visual acuity. So far, determination of the effects of laser radiation on the retina have been mainly dependent on ophthalmological criteria, which do not consider the problem as to how the laser retinal damage is functionally reflected in higher levels of the visual system. Yet more specifically, there is no basic knowledge on the interference with information processing in the visual cortex under these conditions. More specifically, it is not yet known as to what extent these physiological mechanisms are affected by a level of laser radiation which is considered as threshold. In the present program, the destruction of cortical physiological mechanisms following low energy laser retinal radiation was investigated.

Laser retinal effects are currently evaluated mainly by ophthalmoscopy, although recent studies have concentrated on several other approaches for identification and evaluation of these effects. Using electron microscopical techniques, previous investigators have already demonstrated that low levels of laser energy produced ultrastructural alterations in retinal photoreceptors (Ham et al. 1974, Goldman et al. 1975 and Borland et al. 1978). They have determined the threshold of laser energy levels needed for alteration of the photoreceptor outer segments and other retinal components. To determine threshold level for laser induced retinal injury, the behavioral approach has also been used. Zwick (1978), Zwick et al. (1980 a) and Zwick and Bloom (1984) have found that in Rhesus monkeys prolonged viewing of laser sources, even at energy levels far below present laser safety standards, produced permanent changes leading to abnormal visual function.

The above described studies pointed out the need for a physiological criterion for determining the effect of laser radiation on the retina. The electrophysiological approach was first applied by Welch and Priebe (1973), who found changes in the rabbit electroretinogram (ERG) following ruby laser radiation. Similar electroretinographic studies were carried out by Sliney and Wolbarsht (1982). Furthermore, Glickman et al. (1983) described physiological correlates to psychophysical measures of flash blindness in ganglion cells of cats and rhesus monkeys following stimulation with laser pulses of 530 nm. The only study on the effect of retinal induced laser injury on central neurons was performed by Zwick et al. (1980b). They found in turtles irreversible changes in the spectral sensitivity of tectal cells. Receptive fields of these cells constricted and after long exposure even completely disappeared, depending also on the duration and repetition frequency of the exposure. Finally, assessment of ocular hazards of low-power lasers was electrophysiologically carried out by Raybourn and Kong (1984). However, these investigators studied isolated retinæ of turtles in vitro; no attempt was made by them to study the effect on central regions affected by the retinal lesion.

Electrophysiological studies on the effect on higher levels of the mammalian visual system following retinal inactivation by laser radiation are very scarce. Randolph et al. (1982) recorded visual evoked responses (VER) to laser flashes from the visual cortex of

monkeys; they did not detect changes from ED50 to 2 ED50 for q-switched Ruby laser exposure of the retina with spot sizes of 50-500 microns, even when retinal changes were observed at these sites. Furthermore, it was also found in mammals, that using the cortical VER, application of subthreshold laser pulses excited the retina, without inducing any apparent retinal damage (Dawson and Barris, 1978).

Studies aimed at physiologically investigating changes in the visual cortex of mammals following laser induced retinal injury as presently proposed by us have been scarcely performed. The rationale of the present proposal's approach is that the effects on the visual cortex of a mammalian model animal can be related to physiological mechanisms underlying visual perception in humans (Orban, 1984). Laser induced injury to the eye frequently affects neural elements of the retina. As a result of this change there is a chronic absence of visual input to higher levels of the visual system. We hypothesize that this will be functionally reflected in the performance of the visual cortex, since the spatial retinotopic cortical representation of the visual field is affected.

One of the main question with regard to the effect of laser induced retinal injury is the dose-response relationships. We have already described above several previous studies in which the threshold response was physiologically determined for higher levels in the visual system of various species. In the present study we physiologically characterized the threshold response of the visual cortex in a mammalian model.

In addition to providing new evidence on processing of visual information from the injured lased retina by the visual cortex, the conclusions of the present study can be applied to the improvement of laser safety standards and the diagnosis of the damage produced.

1. The effect of Nd:YAG laser induced retinal lesions on the electroretinogram (ERG).

Methods

The domestic cat (*Felis catus*) which was utilized in the present study was of a genetically homogenous group originated from a mixture of Abyssinian and various home cats of Ciba-Geigy, AG (Basel, Switzerland). These cats were SPF inbred for the last 15 years at Tel-Aviv University central animal house. Cats have been widely accepted in the world as a mammalian model for studying the physiological properties of the eye and the visual cortex. In addition, the cost of cats is 10% of that of monkeys commonly used as laboratory animals. Adult cats of both sexes were studied (3 kg; age: >1 year). The cats were kept in cages and all the appropriate conditions provided in accordance with the standard regulations. Room temperature was 23°C, relative humidity 50%, photoperiod 14 hrs light and 10 hrs dark (illuminance in the cages: 100 ft-candles; measured with Megatron photometer); ventilation allowed room air to change over 20 times per hour. The environmental conditions were all automatically controlled. The rearing conditions and maintenance thus adhered to the Guide for the Care and Use of Laboratory Animals (PHS Pub. No. 80-23, 1980), prepared by the Committee on Care and Use of Laboratory Animal Resources, National Research Council, U.S.A. Our animal facilities and conditions are also in conformance with the GLP (The United States Good Laboratory and Practices Regulations).

The laser device used by us in the present study was of the Neodymium:YAG type. The Nd:YAG laser is a solid state laser capable of producing a pulsed or continuous infrared beam at the wavelength of 1064 nm. The pulsed Nd:YAG laser can cause damage to the retina and choroid, particularly when treating the vitreous at a distance of 3 mm or closer to the retinal surface. With direct treatment of the retina, threshold injuries appear to cause localized damage within the photoreceptor cells and retinal pigment epithelium; higher energy levels cause choroidal hemorrhages. We thus decided in the present study to define the physiological features, in an animal model, of pulsed Nd:YAG laser treatment applied to the retina at threshold and subthreshold energy levels. Energy levels were in the range of 0.1-1.0 millijoules (mJ) per pulse. This is under the threshold level in view of the fact that in rabbits and monkeys energy levels (Nd:YAG laser) less than 4-12 mJ did not produce ophthalmoscopically visible chorioretinal damage (Bonner et al., 1983); this has been confirmed for rabbits (9-14), under the same physical conditions (Brown et al., 1986). In our laser system the retina was lased by a single pulse at a time. The spot diameter was 30-50 micron. The number of pulses varied between cats, and ranged from 1 to 20 per eye; in 2 cats only 100 pulses were applied. All eyes were dilated with Atropine sulfate (1%), and following anesthesia with Ketamine (15 mg/kg, i.m.) supplemented with Xylazine (Rompun, 2 mg/kg, i.m.), were exposed to the laser radiation on the area centralis. Single or multiple exposures were applied at an eccentricity of 0-50 from the center of the area centralis. The target region for laser exposure was determined by direct ophthalmoscopic viewing. The location of the lesioned retinal area after the laser radiation was determined ophthalmoscopically by direct viewing.

The numbers of cats electrophysiologically studied are listed in Tables 1-2; adult cats of both sexes were studied. The cats were subjected to the electrophysiological examinations, either acutely (1 week) or chronically (4-8 weeks) studied after the termination of the exposure to laser radiation (Table 3). The cats were physiologically examined 1-3 times for each eye; the results thus reflect the average of these examinations. However, in several cats a more longitudinal study was performed in order to follow recovery; these cats were electrophysiologically studied up to 5 times over a period of 4-6 weeks. The ERG was recorded following Ketamine and Rompun anesthesia and pupillary dilation with Atropine. The nictitating membrane was retracted following application of Phenylephrine HCL 10%. For the electrophysiological sessions the cats were restrained on a stereotaxic apparatus following the anesthesia. To further prevent pain, all head regions in contact with the stereotaxic apparatus were injected with local anesthetic. The cats were continuously supervised throughout the experiments by monitoring and recording the ECG. The body temperature was electronically regulated using rectal probe and feedback systems.

For the ERG recordings, contact lens electrodes (Medical Workshop, Holland) were used; the indifferent electrode was a needle inserted under the skin. There was no special attempt to separate between the rod and the cone subsystems; however, a sufficiently long period of dark adaptation (10 minutes) was provided to let the scotopic mechanism (representing the rod subsystem) dominate the response. Thus, the ERG was recorded (simultaneously from both eyes) during a significant part of the scotopic phase of the dark adaptation period. After the adaptation

period, five stroboscopic flashes from a Grass PS 22 Photo-Stimulator were given at intervals of 2 minutes. The stroboscope was synchronized with a PDP 11/23 computer and operated by a specially devised computer program. In order to enable diffuse light to reach the retina, the lamp was covered with translucent plastic cover; furthermore, diffusion was facilitated by the large distance (100 cm) of the stroboscope lamp from the retina. A medium level of light intensity (I-4) was used; saturation of the ERG was thus prevented in our study. Following amplification and filtration by a Grass P5 A.C. Pre-Amplifier (bandwidth: 0.1Hz-1.0 KHz) the ERGs were averaged by a PDP 11/23 computer (DEC) with our program (Fig. 1). The ERGs were then plotted on a Hewlett-Packard X-Y Recorder (Fig. 3).

Analysis of the ERG was made in the same way for the normal and for the experimental eyes. The normal eyes had the same ERG pattern and values as those obtained for normal cats currently used by us for electroretinographic studies. Thus, the exposed eyes could be statistically regarded as the normal eyes before the exposure to laser radiation. Measurements of the ERG amplitude and the latency values, respectively, were carried out using special measuring devices of the program. Calculations of the various ERG parameters were performed by comparing and averaging the response of the lased eye with the response of the fellow normal eye of the same cat. An example of computer calculations of the various ERG components and the experimental conditions is seen in Fig. 1.

Results and conclusions

The ERG was consistently smaller in amplitude in the affected eye in comparison to the normal fellow eye. This is indicated by the fact that the ERG of the lased eye was smaller in most of the animals studied, both in its a- and b-wave amplitudes, in comparison to that of the normal eye (Table 1). The average difference between the ERG amplitudes obtained to stimulation of the normal and the lased eye was higher than the average difference found for the ERG response to stimulation of the right and the left eye of the normal control cats. It is interesting to note here that the relatively low level of laser radiation applied induced a change in the retinal response. Our final analysis of the results indicate no linear relationship between the number of laser pulses to which the retina was exposed and the amplitude of the ERG. Exposing the retina to 3 pulses was not less effective than 15 pulses, despite the fact that the latter was at much higher energy level (pulses of 0.5 versus 0.1 mJ). Furthermore, no relationship was found as function of energy level applied. Finally, it was found that the acute and the long chronic cats gave similar electrophysiological results (the survival times of the various cats are described in Table 2). Thus, no recovery with time was so far found with regard to threshold and subthreshold levels of laser retinal radiation.

Our main conclusions are the following:

- 1) The electroretinogram (ERG) indicates retinal damage to exposure with threshold levels of Nd:YAG laser radiation.
- 2) Since the retinal area radiated by laser in our study was small, the actual damage found is considerably larger than what would be expected from ophthalmoscopic observations.
- 3) The damage induced in the retina, although it is difficult to infer whether it is related to the specific effect of multiple

exposures, is irreversible, since no recovery with time was found.

4) For the ERG to serve as a diagnostic tool in determining laser induced damage, it has to be supplemented by other parameters such as visual acuity and visual fields measurements. This is true even to an extent that the retinal damage has a significant effect on vision in the central portion of the visual field.

2. The effect of Nd:YAG laser induced retinal lesions on the visual evoked response (VER).

Methods

The experimental animals used were adult cats, as above described. VER recordings were made from the primary visual cortex, area 17. Recordings were carried out acutely (1-4 days after the exposure to the laser radiation) and chronically (8 weeks after the exposure) (Table 2). Detailed techniques of exposure to the laser radiation, anesthesia, surgery, visual stimulation, and computation were described in the previous section.

For the electrophysiological recording procedures, a special head implant was installed on the animal's occipital bone, and positioned above visual cortex area 17. The implant was attached under full anesthesia to the skull with screws and dental cement using an array of 2-3 holes which were produced in the exposed skull, for each experimental cat and for each hemisphere. During the recording sessions one of the holes was penetrated with a stainless steel metal electrode to be in direct contact with the surface of the visual cortex. At the end of implantation session the animal received antibiotic treatment for a week. The visual cortex was electrophysiologically studied by recording the visual evoked response (VER). The direct contact of the electrode with the cortex insured a small signal/noise ratio and stability of the VER during the various recording sessions with the same animal. The indifferent electrode was inserted under the skin.

The responses were accumulated during stimulation with 40-100 stroboscopic flashes and averaged by a PDP 11/23 (Digital) computer using a special program for data acquisition. Analysis of the VER was made in the same way for the normal and the experimental eyes and cats. Measurements of the VER amplitudes and the latency values, respectively, were carried out using special measuring devices of the program. Calculations of the various VER parameters were performed by comparing and averaging the response of the lased eye with the response of the fellow normal eye of the same cat. For the VER analysis, the peak amplitudes of the three main components were averaged (P1-P3) (Fig. 4). An example of computer calculations of the various VER components and the experimental conditions is seen in Fig. 2.

Results and conclusions

The VER amplitude following stimulation of the normal eye was consistently higher than that resulting from stimulation of the lased eye (Table 2). The average difference between the VER amplitudes obtained to stimulation of the normal and of the lased eye was remarkably higher than the average difference found for the VER response to stimulation of the right and the left eye of the normal control cats. However, we found no relationship between the number of laser pulses to which the retina was exposed and the amplitude changes in the VER. As to the energy level, no consistent

difference was found over the range of 0.1 to 1.0 mJ for the various number of laser pulses applied. The same conclusion was reached regarding the effect of survival time; no clear consistent change as function of recovery time can be seen.

Our main conclusions are the following:

1) The visual evoked response (VER), indicates retinal damage following exposure to Nd:YAG laser radiation at threshold and subthreshold energy levels.

2) Since the retinal area radiated by laser in our study was small, the actual damage found is considerably larger than what would be expected from ophthalmoscopic observations.

3) The retinal induced damage, in spite of the difficulty to infer whether related to the multiple exposures, is irreversible, since no recovery with time was found.

4) That the VER is more prominently affected than the ERG, is due to the fact that the central retina - where the lesion was purposely made - is represented on a large cortical area while the effect on ERG amplitude is linearly related to the retinal area affected.

5) For the VER to serve as a diagnostic tool in determining the extent of laser retinal induced damage, it has to be supplemented by other parameters such as visual acuity measurements. This is even true under conditions where the retinal damage has a significant effect on vision in the central portion of the visual field.

3. Histological and morphological changes of the lased retina.

Methods

Upon termination of a complete series of physiological experiments on each animal it was injected with a high dosage of sodium pentobarbital, i.v. (under constant monitoring of the EEG). Thus, disposition of the animals was carried out by a painless induction of death.

Histological studies of the lased eyes were performed in order to verify the extent of the laser effect on the retina of each exposed cat. For this purpose the lased eyes were injected with 10% buffered Formalin during the anesthesia; in several cats the normal eye was studied also for comparison. After a period of four weeks which allowed fixation of the eyes they were embedded in paraffin, sectioned (10 microns) and stained in Haematoxylin Eosin. Light microscopy studies of the histological preparations were carried out in the Histology Laboratory of the Eye Institute.

Results and conclusions

The most common finding immediately ophthalmoscopically observed after the exposure to the laser radiation was a loss of pigmentation in the lesioned site, referred in Table 3 as discoloration. At a more advanced stage a hemorrhage was found at the lesioned site. When the energy level was low only a brownish pigmentation was ophthalmoscopically visible. However, in more severe lesions, a hemorrhage was more clearly visible; then the choroid was also involved. Only in the animals in which 100 retinal lesions were made, a wide hemorrhage was ophthalmoscopically observed with discoloration of the whole central retinal area (area centralis).

It is important to note here that in many cases the same laser pulse (i.e., same physical parameters) and similar retinal locations, induced different effects (Fig. 6). This was reflected in the appearance of a remarkable hemorrhage in one lesion and slight discoloration in the neighboring one. In connection with this, it was found that under the same physical parameters of laser radiation, variability occurred not only in the the same eye but between different animals. For instance, while in most of the cats, pulses of 0.1 mJ were effective, in cat no. 1806 there was no change after 20 pulses at that energy level. When this was followed by 2 pulses of 0.5 mJ, no change was observed; only after exposing the same eye to one pulse of 1.0 mJ a slight discoloration appeared.

The effect of the laser lesion on the retina remained for a long period of time. For instance, in cat 1811 we found that out of 6 retinal lesions produced, after 6 weeks 4 of them were still clearly observed.

As to the histological findings, it was found that in the severe cases the retina was detached from its supporting tissue in the lased parts, resulting in ruptures; however, some contact remained in the periphery of the lesion (Fig. 5). When the effect of the lesion was mild, a rupture was found only in the photoreceptor layer following the destruction of the photoreceptors; no damage was then found in the pigment epithelium layer. We found that the lesion was usually more severe in parts of the eye where the choroid tissue was loose. In several cases a rupture was found in the pigment epithelium and in others only in the choroid. However, in many cases no histologically observable damage occurred in the lesioned sites, although we can not exclude the possibility that ultrastructural changes had occurred there, affecting the retina functionally.

Tables

Table 1: Summary of ERG* data of individual cats.

Cat no.	<u>Eye studied</u>				<u>YAG laser conditions</u>		
	<u>Lased</u>		<u>Normal</u>		<u>No. of pulses</u>	<u>Interval between pulses (min)</u>	<u>Energy (mJ)</u>
	<u>ERG Amplitude b-wave</u>	<u>ERG Amplitude a-wave</u>	<u>ERG Amplitude b-wave</u>	<u>ERG Amplitude a-wave</u>			
1818	119	31	150	39	3	2	0.1
1819	209	31	212	28	3	2	0.1
1813	289	96	291	97	6	2	0.2
1814	552	114	555	115	6	2	0.2
1816	337	28	421	58	15	2	0.5
1815	223	21	197	20	15	2	0.5-0.6

Normal controls:

	<u>Left</u>		<u>Right</u>	
1786	405	155	393	129
31	709	252	704	254
3753	400	112	412	125
20284	224	88	224	88

* ERG amplitude was calculated in microvolts.

** Energy per pulse.

Table 2: Summary of VER* data of individual cats.

Cat no.	<u>Eye studied</u>		<u>Normal</u> Pl-P3 Amplitude	<u>YAG laser conditions</u>		Interval between laser exposure & VER recording
	<u>Lased</u> Pl-P3 Amplitude			<u>No. of</u> pulses	<u>Energy</u> (mJ)	
1801	19		18	1	0.1**	4 days
1809	31		56	1	0.1	2 days
1807	58		55	1	0.1	3 days
1817	I 61		58	3	0.1	1 month
	II 51		69			
1819	I 19		30	3	0.1	1 month
	II 29		34			
1818	I 63		82	3	0.1	6 weeks
	II 117		121			
1805	16		21	7	0.1	1 day
1808	15		27	7	0.1	1 week
1814	I 10		14	6	0.2	1 week
	II 11		22			
1813	I 16		18	6	0.2	1 month
	II 8		10			
18.2	10		10	6	0.2	1 week
1803	15		11	1	0.5	1 day
1802	16		26	1	0.5	1 day
1811	77		88	6	0.5	4 days
1816	51		30	15	0.5	2 months
1815	I 18		13	15	0.5-0.6	1 week
	II 14		13			
1806	47		37	20	0.1-1.0	1 day

cont. Table 2:

Normal controls:

	<u>Left</u>	<u>Right</u>
1793	24	25
1790	27	24
1791	43	47
1794	7	6

* VEP amplitude is calculated in microvolts.

** Energy per pulse.

I,II, results collected in two different experiments from the same cat.

Table 3:

Summary of morphological and histological changes following Nd:YAG laser radiation on the retina of cats. All retinal exposures were carried out at the area centralis.

<u>Cat no.</u>	<u>Number of pulses</u>	<u>Energy (mJ)</u>	<u>Condition of laser retina</u>
1801	1	0.1**	small hemorrhage
1807	1	0.1	discoloration central hemorrhage
1809	1	0.1	small discoloration
1817	3	0.1	small discolorations
1818	3	0.1	sub-retinal hemorrhage
1819	3	0.1	discoloration sub-retinal hemorrhage

cont. Table 3:

1805	7	0.1	no hemorrhage
1808	7	0.1	no hemorrhage
236	100	0.1	extensive hemorrhage
232	100	0.1	extensive hemorrhage
1806	20	0.1-1.0	small discolorations (needle heads) no hemorrhage
1812	6	0.2	small discolorations
1813	6	0.2	no hemorrhage
1814	6	0.2	no hemorrhage
1802	1	0.5	no hemorrhage
1803	1	0.5	no hemorrhage
1811	6	0.5	small discolorations
1804	7	0.5	no hemorrhage
1816	15	0.5	small hemorrhage
1815	15	0.5-0.6	no hemorrhage
1810	LE 23	0.1 mW	central edema
	RE 23	0.3 mW	strong discolorations
	(Argon laser; 0.1 sec.; spot size: 100 microns)		

* Area centralis.

** Energy per pulse.

mW, milliwatts.

Explanations for figures:

Fig. 1: Example of computerized Electroretinogram (ERG) recorded from experimental cat (no. 1816), following stimulation of the lased (LAS) and the normal (NOR) eye. LA, LB, a-wave and b-wave latency, respectively; AA, AB, a-wave and b-wave amplitudes, respectively. For additional details regarding this cat see Tables 1- 3.

Fig. 2: Example of computerized Visual Evoked Response (VER) recorded from visual cortex area 17 of an experimental cat (no. 1819), following stimulation of the normal (2A, NOR) and lased (2B, LAS) eye. L, latency; A, amplitude. The peak responses of the VER are numbered in the order of their appearance. For other conventions see legend to Fig. 1. For additional details regarding this cat see Tables 1-3.

Fig. 3: ERG recorded from experimental cat (no. 1816), following stimulation of the lased (LAS) and the normal (NOR) eye. A, a-wave; B, b-wave; ms, milliseconds. For additional details regarding this cat see Tables 2 and 3.

Fig. 4: VER recorded from visual cortex area 17 of an experimental cat (no. 1809), following stimulation of the lased (LAS) and the normal (NOR) eye. 1,2,3, peak responses analyzed for this cat. For additional details regarding this cat see Tables 2 and 3.

Fig. 5: Cross sections through the lased eye of an experimental cat (no. 1816). A, a large rupture (R) is seen in the choroid (C). B, a small rupture is seen in the photoreceptor (P) layer. Scale: 500 microns. For additional details regarding this cat, see Tables 2 and 3.

Fig. 6: The distribution of laser lesions in the retinae of experimental cats. A, schemes of the main retinal blood vessels and the optic disk presented on the left side and the lesions on the right side (empty circles indicate discoloration; full circles indicate hemorrhage). The number of each animal is also indicated. For additional details regarding these cats, see Tables 1-3. B, a photograph of the retinal surface of one of the lased cats; a hemorrhage (arrow) is clearly seen right of the optic disk (arrow).

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FIGURE - 1.

Identification of experiment: 1816I

- 1) Number of channels: 2
- 2) Channel numbers: 0 1
- 3) Time range: 150 msec
- 4) Rejection window: 1000.00 microvolts
- 5) Number of flashes: 5
- 6) Flash intervals:
 1. 0 m 30.0 s
 2. 0 m 30.0 s
 3. 0 m 30.0 s
 4. 0 m 30.0 s
 5. 0 m 30.0 s
- 7) The experiment's data will be saved on file 1316I.DAT
- 8) Raw data saved? : Y

Name/number of experiment : I-ERG
Name of investigator : AUL
Number of animal : 1816
Flash light intensity : I-4
Bandwidth : 0.1HZ-1KHZ
50 c/s filter, in or out : OUT
Distance of lamp from eyes : 100CM
Background illumination : DARK
Calibration signal frequency : 10HZ

DATE;

The **NEW** measurements for channel 0 : NOR

LA	-	57.005	Milliseconds
AA	-	-58.291 ± 2.642	(SE) Microvolts
LB	-	57.005	Milliseconds
AB	-	421.139 ± 8.995	(SE) Microvolts

The **NEW** measurements for channel 1 : LAS

LA	-	19.890	Milliseconds
AA	-	-28.460 ± 0.874	(SE) Microvolts
LB	-	67.210	Milliseconds
AB	-	337.333 ± 4.516	(SE) Microvolts

FIGURE - 2A. NOR

Identification of experiment: 18191

- 1) Number of channels: 1
- 2) Channel numbers: 0
- 3) Time range: 250 msec
- 4) Rejection window: 1000.00 microvolts
- 5) Number of flashes: 39
- 6) Flash intervals:

1. 0 m 4.0 s	2. 0 m 5.5 s	3. 0 m 5.0 s	4. 0 m 5.3 s
5. 0 m 5.1 s	6. 0 m 5.6 s	7. 0 m 3.7 s	8. 0 m 4.0 s
9. 0 m 5.5 s	10. 0 m 5.4 s	11. 0 m 5.4 s	12. 0 m 4.0 s
13. 0 m 3.9 s	14. 0 m 5.2 s	15. 0 m 5.0 s	16. 0 m 3.6 s
17. 0 m 4.9 s	18. 0 m 5.2 s	19. 0 m 5.3 s	20. 0 m 5.1 s
21. 0 m 5.5 s	22. 0 m 3.7 s	23. 0 m 4.9 s	24. 0 m 4.6 s
25. 0 m 4.3 s	26. 0 m 4.8 s	27. 0 m 4.6 s	28. 0 m 4.4 s
29. 0 m 4.1 s	30. 0 m 4.9 s	31. 0 m 5.1 s	32. 0 m 4.9 s
33. 0 m 3.6 s	34. 0 m 4.2 s	35. 0 m 5.3 s	36. 0 m 4.1 s
37. 0 m 3.6 s	38. 0 m 5.0 s	39. 0 m 3.8 s	
- 7) The experiment's data will be saved on file 18191.DAT
- 8) Raw data saved? : Y

Name/number of experiment : 1-VEP
 Name of investigator : RAUL
 Number of animal : 1819
 Flash light intensity : 1-4
 Bandwidth : 1HZ-100HZ
 50 c/s filter, in or out : IN
 Distance of lamp from eyes : 100CM
 Background illumination : DARK
 Calibration signal frequency : 10HZ

DATE:

THE GAIN VALUE IS CALIBRATED.
 INTERNAL GAIN FOR CHANNEL 0 WAS SET AT x2
 THE CONVERSION FACTOR IS 0.130378 Microvolts/Bit

The measurements for channel 0 :

LP1	-	27.258	Milliseconds
AP1	-	-16.291 ± 1.882	(SE) Microvolts
LP2	-	49.206	Milliseconds
AP2	-	38.171 ± 11.396	(SE) Microvolts
LP3	-	69.738	Milliseconds
AP3	-	18.885 ± 14.907	(SE) Microvolts
LP4	-	107.262	Milliseconds
AP4	-	24.371 ± 9.386	(SE) Microvolts
LP5	-	155.406	Milliseconds
AP5	-	26.617 ± 7.567	(SE) Microvolts

FIGURE - 2B. LAS

Identification of experiment: 1819J

- 1) Number of channels: 1
- 2) Channel numbers: 0
- 3) Time range: 250 msec
- 4) Rejection window: 1000.00 microvolts
- 5) Number of flashes: 39
- 6) Flash intervals:

1. 0 m	4.1 s	2. 0 m	3.8 s	3. 0 m	4.7 s	4. 0 m	4.1 s
5. 0 m	4.5 s	6. 0 m	4.9 s	7. 0 m	5.1 s	8. 0 m	5.1 s
9. 0 m	4.9 s	10. 0 m	3.7 s	11. 0 m	4.9 s	12. 0 m	4.0 s
13. 0 m	4.9 s	14. 0 m	5.6 s	15. 0 m	3.6 s	16. 0 m	4.1 s
17. 0 m	4.4 s	18. 0 m	3.7 s	19. 0 m	5.2 s	20. 0 m	4.6 s
21. 0 m	5.0 s	22. 0 m	5.3 s	23. 0 m	5.3 s	24. 0 m	4.7 s
25. 0 m	4.5 s	26. 0 m	3.7 s	27. 0 m	3.7 s	28. 0 m	3.6 s
29. 0 m	4.7 s	30. 0 m	4.1 s	31. 0 m	4.2 s	32. 0 m	4.8 s
33. 0 m	5.4 s	34. 0 m	3.7 s	35. 0 m	4.4 s	36. 0 m	5.3 s
37. 0 m	4.2 s	38. 0 m	3.9 s	39. 0 m	4.2 s		
- 7) The experiment's data will be saved on file 1819J.DAT
- 8) Raw data saved? : Y

Name/number of experiment : J-VEP
 Name of investigator : RAUL
 Number of animal : 1819
 Flash light intensity : I-4
 Bandwidth : 1HZ-100HZ
 50 c/s filter, in or out : IN
 Distance of lamp from eyes : 100CM
 Background illumination : DARK
 Calibration signal frequency : 10HZ

DATE:

THE GAIN VALUE IS CALIBRATED.
 INTERNAL GAIN FOR CHANNEL 0 WAS SET AT x2
 THE CONVERSION FACTOR IS 0.130591 Microvolts/Bit

The measurements for channel 0 :

LP1	-	20.886	Milliseconds
AP1	-	-13.586 ± 2.063	(SE) Microvolts
LP2	-	51.330	Milliseconds
AP2	-	21.815 ± 6.546	(SE) Microvolts
LP3	-	71.154	Milliseconds
AP3	-	11.576 ± 7.909	(SE) Microvolts
LP4	-	86.730	Milliseconds
AP4	-	17.995 ± 6.839	(SE) Microvolts
LP5	-	137.706	Milliseconds
AP5	-	15.992 ± 6.063	(SE) Microvolts

FIGURE 3

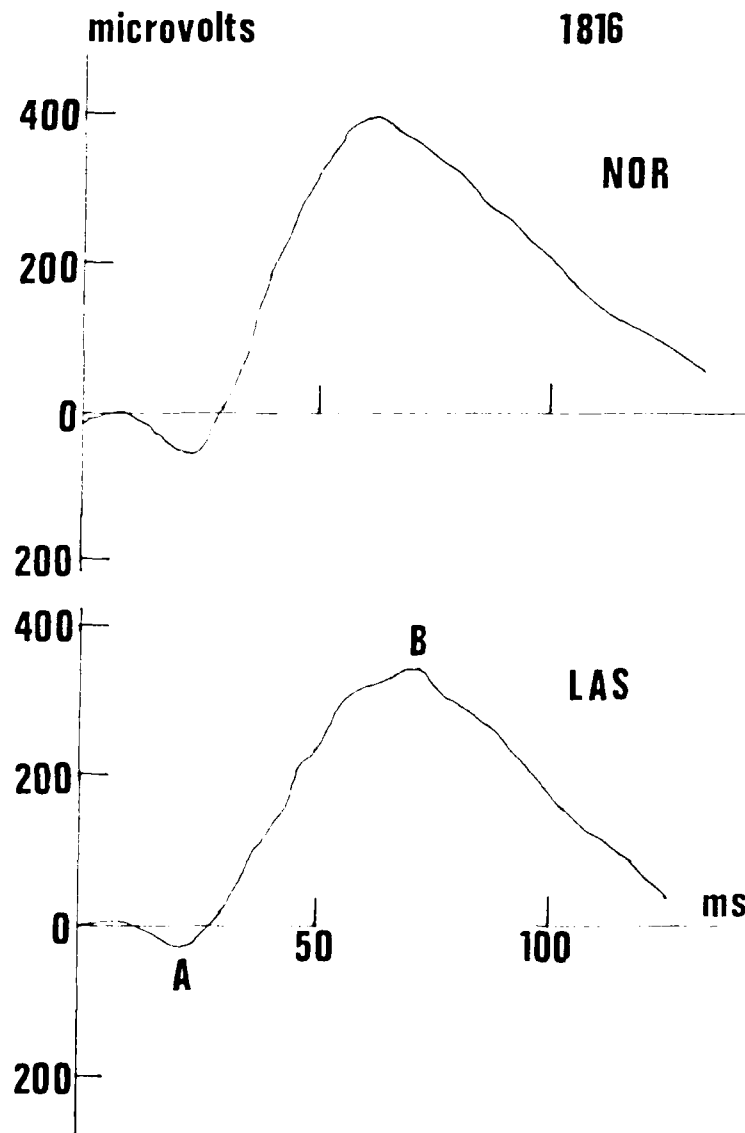


FIGURE 4

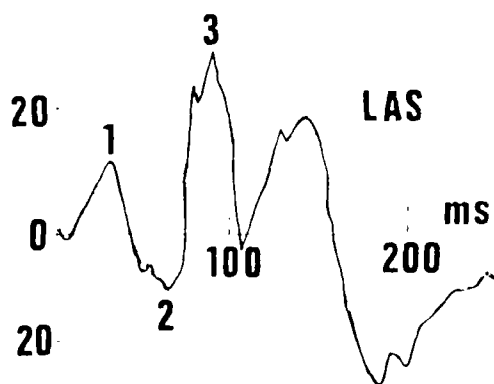
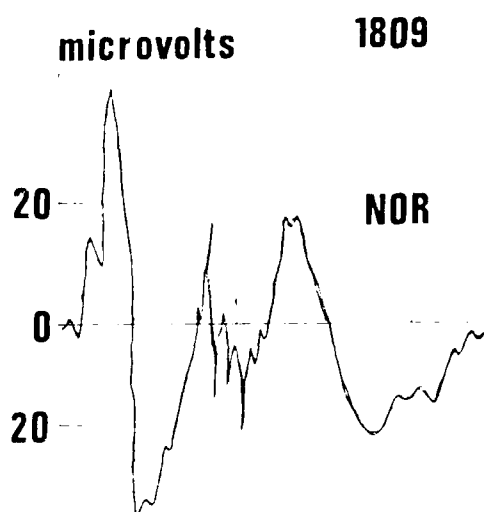


FIGURE 5

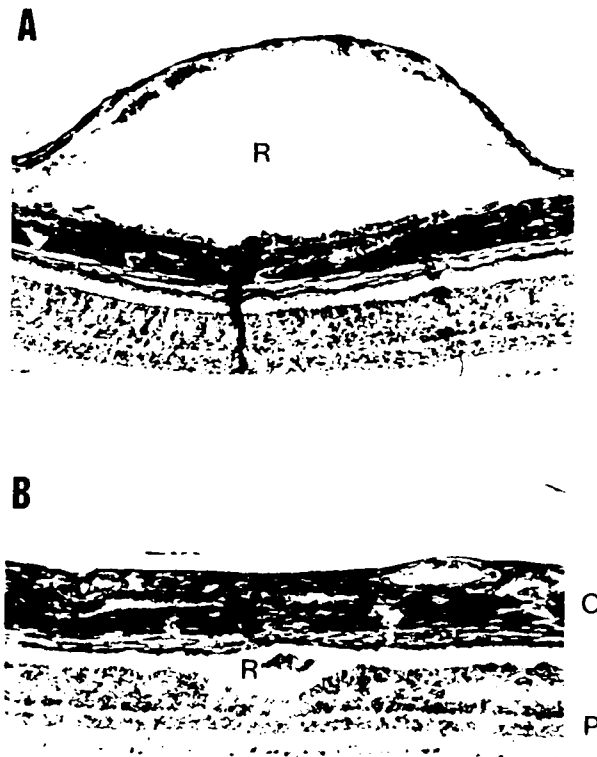
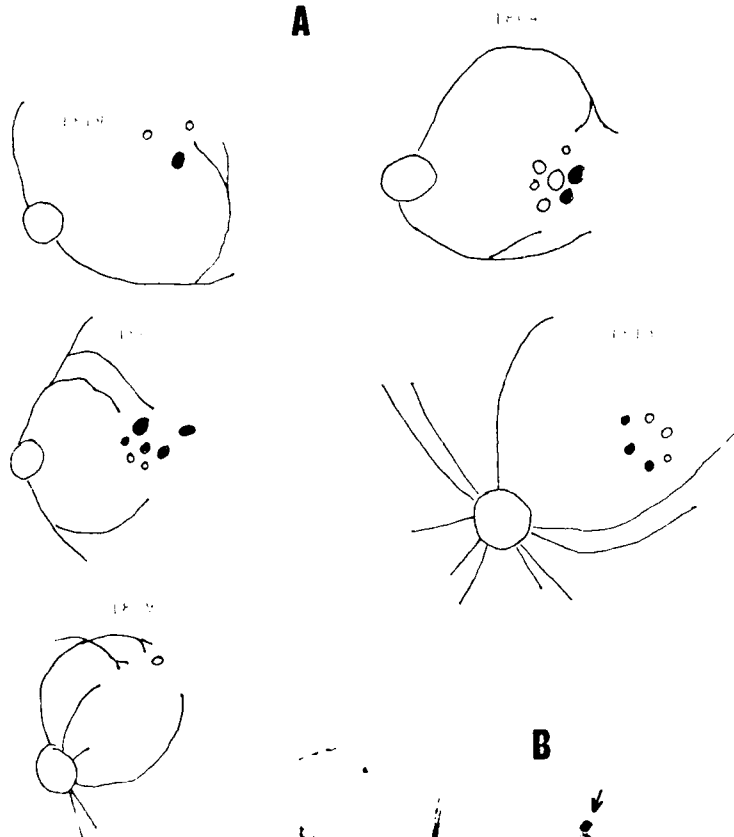


FIGURE 6

A



B

